This method uses an infrared plethysmograph observing any changes in the unstressed volume of the finger arteries, mounted in an inflatable cuff providing at each instant a counter pressure sufficient to just counterbalance intraarterial pressure. Since this requires dynamic control of cuff pressure it is performed by a wideband servo system which uses the plethysmogram as one input. The other input is the proper unstressed finger arterial volume level which is determined automatically by an expert system programmed on a microcomputer built into FINA PRES.

With respect to the transcranial Doppler ultrasonic recording of cerebral blood flow this seems to us an attractive method for studying changes in cerebral blood flow, whereby we leave open the question of which circulation is more peripheral, the one in the finger or the one in the cerebrum. However, the discordance between central blood flow and systemic blood pressure, in particular in patients with autonomic failure has been well noted and has been attributed to a change in autoregulation of the cerebral circulation. 5 In the light of these facts, the statement of Drs Reinecke and Langohr that “measurements of cerebral artery flow velocity allow a better visualisation of autonomic reflexes in a more central part of the circulation...” cannot be unmodified. Their fine technique may, however, prove a promising clinical tool in studying the instantaneous and varying discordance between flow and pressure in different parts of the circulation in combination with the equally non-invasive registration of continuous blood pressure in the finger.

Recurrence, hyponatraemia and neuroleptic malignant syndrome

Sir: We found the case-report by Gibb et al describing recurrent neuroleptic malignant syndrome in association with hyponatraemia 1 very interesting. However, we do not agree with the authors on several points. The authors maintain that recurrence of neuroleptic malignant syndrome has not been reported despite reinduction of neuroleptic therapy on frequent occasions after single episodes. A careful review of published literature gives a totally different picture. 2 - 4 Recurrence was noticed in six out of eight cases when rechallenge was done with the same drug. 3 Rechallenge with drugs of the same milligram potency as the offender (6 cases) resulted five times in recurrent neuroleptic malignant syndrome with two fatalities. 3 On the other hand, rechallenge with lower potency antipsychotics, particularly thioridazine, was safe in nine out of 10 cases. 3 If the rechallenge is attempted with the same drug but at a slower loading rate, there may not be any recurrence. 4 - 6 Relapse has also been observed in cases where the treatment was discontinued prematurely. 7 - 8 Besides this we wonder whether the diagnosis of neuroleptic malignant syndrome was made prospectively or retrospectively. There are several indicators which suggest that the diagnosis was retrospective. The clinical details provided in the first presumed episode of neuroleptic malignant syndrome are insufficient to make a diagnosis of neuroleptic malignant syndrome. No alteration in consciousness was noted in the first “episode”. Altered consciousness is essential for diagnosing neuroleptic malignant syndrome. 2 - 4, 9 The authors made no comments regarding presence or absence of autonomic dysfunction in the first “episode”. We have no information about serum CK levels in the first episode. No muscle biopsy findings are available for either of the episodes. Moreover, in both the “episodes” the patient was not given any specific treatment for neuroleptic malignant syndrome. One of the problems which has been faced in analysis of cases of neuroleptic malignant syndrome is failure on the part of the authors to provide a complete clinical description. 2 It has been proposed that the published reports of neuroleptic malignant syndrome should not be accepted uncritically. 10

We feel that the authors should have provided more clinical details before making a diagnosis of “recurrent” neuroleptic malignant syndrome if such a diagnosis was made prospectively.

ADITYANJEE

References


Gibb et al reply:

Dr Adityanujee has challenged our statement that recurrent neuroleptic malignant syndrome (NMS) has not been described previously, by citing three papers that apparently conflict with this. 1 - 3 One paper 1 discusses the possibility of recurrent NMS without referring to such a case, while the other two 2, 3 do not mention in their reviews of the literature uncomplicated cases in which entirely separate episodes of NMS are described. The cases referred to are as follows. One case was an acute dystonic reaction, drugs were stopped and no rechallenge done. 4 One case was an NMS-like reaction following withdrawal of tetrabenazine, but there was no recurrence when haloperidol was started on the 42nd day. 5 In five cases NMS was provoked before full recovery, when drugs were restarted before the tenth day. 6 - 9 Furthermore two of these cases may not have had recrudescence of NMS for there was little or no fever or record of rhab.-
Matters arising
domyolysis,7 and in only one of the five cases were events adequately documented.9 In fact in one case thiordiazine was started after an interval of one month without ill-effect.6 Another report described autonomic disturbances, of uncertain significance, occurring before and after an episode of NMS.10 In two other cases illness was separated by a 6 month interval. One of these, with a possible history only, was complicated by multiple seizures.11 The other may have had NMS but the febrile episodes occurred with Klebsiella pneumonia and Staphylococcal septicemia.12 The source of two other referenced cases is unclear.
Shalev and Munitz2 and Dr Adityaneej raise the important question of whether neuroleptic drugs can safely be used after an episode of NMS. Clearly if medication is restarted before recovery then relapse will occur. Abandoning full treatment of NMS is not likely to be helpful either. There is, however, no previously documented case acceptable to Dr Adityaneej's critical eye, where NMS has occurred after full recovery, allowing an interval of more than one month, for example. Indeed a tendency for non-recurrence is the generally accepted dogma,13 although under-recognition and under-reporting are likely. There is no reason why recurrences could not occur and if a patient requires further neuroleptic medication then caution suggests that neuroleptics should be started after at least three weeks recovery, preferably with gradual increments made under observation, of a less potent neuroleptic with intrinsic anticholinergic properties.14
In our case report15 fever, muscular rigidity, rhabdomyolysis and hyponatraemia occurred on two occasions seven months apart and without evidence of other contributory disease.14 Impaired consciousness should be a relatively late sign of NMS and "autonomic disturbances" likewise probably reflect severe illness alone. The interesting aspect of this case is the association of NMS with hyponatraemia and a stable drug regime, whereas in 53 of 56 cases NMS occurred after starting or increasing the dose of neuroleptics.15,16 Two other patients with hyponatraemia have now been described19,17 and in one of these cases NMS recurred, after 8 months on a stable drug regime, as in our case.17 The reason why dilutional hyponatraemia rather than an increase in neuroleptic medication may precipitate NMS is unclear. Conceivably an abrupt lowering of extracellular sodium concentration could lead to pre- or postsynaptic changes at the striatal dopaminergic synapse, with an effect analogous to the excessive stimulation of dopamine receptors postulated in NMS.14

References

Distribution of multiple sclerosis in the United Kingdom

Sir: The excellent update of the UK distribution of multiple sclerosis by Swingler and Compton1 emphasised the gradient in the association of HLA-DR2 and clinical multiple sclerosis prevalence which they showed declining progressively from SE England to NE Scotland. Their fig 11 showed the frequency of DR2 to be constant at 50% in multiple sclerosis cases throughout the UK whereas in controls it rose progressively from South to North.

My own general practice figures of 14% multiple sclerosis patients in an NHS list of 3,000 gives a remarkable prevalence of 500/105 and has prompted a postal survey of other general practitioners in the New Forest area which showed 148 cases of multiple sclerosis in 140,765 people, giving a prevalence rate of 105/105. However, from this and four practices with Disease Registers the figure was 62 multiple sclerosis patients in 36,115 = 172/105 (four other practices with out such registers also reported figures giving prevalence rates of 143, 143, 145 and 154 per 105 in a further population of 17,700). These figures are exceeded worldwide only by those in the Orkney and Shetland Islands whose acid terrain of heather and wet peat is similar to the Forest.

HLA-status has not yet been defined in these cases but in unpublished figures obtained from the Wessex Region's Blood Transfusion Services, HLA-DR2 antigens are found in only 15% of 1,174 healthy volunteers for bone marrow transplantation in this region. This compares with the UK Transplantation Service's nationwide figures of 30% in those typed as cadaveric organ donors. The low Wessex figure for DR2 would suggest that this observed cluster of patients with multiple sclerosis is not genetically determined.

Using the DHSS Prolonged Study Leave scheme for general practitioners, I am now undertaking a survey of the multiple sclerosis patients (and controls) in the New Forest, designed to look at environmental factors, with specific interest in any significant differences pre-puberty, in the residential or recreational habitats, and in animal contacts. If environmental histories are not significantly different in the two groups then the HLA-DR2 prevalence will be sought. As Swingler and Compton pointed out, if all are exposed to the same environment then only those with susceptible genotypes will develop morbidity. Their graph would suggest that the 15% HLA-DR2 rate mentioned above in the healthy Wessex